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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,424	06/21/2001	Karl Kavalkovich	640100-426	4226

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EXAMINER

NAFF, DAVID M

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 09/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

9/83142f

Applicant(s)

Kavakovich et al

Examiner

R/af

Group Art Unit

1657

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 6/21/01

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1 - 11 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

☒ Claim(s) 1 - 11 is/are rejected.

Claim(s) _____ is/are objected to.

Claim(s) _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The proposed drawing correction, filed on _____ is approved disapproved.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been received.

received in Application No. (Series Code/Serial Number) _____

received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____

Attachment(s)

Information Disclosure Statement(s), PTO-1449, Paper No(s).

Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

Notice of Informal Patent Application, PTO-152

Notice of Draftsperson's Patent Drawing Review, PTO-948

Other _____

Office Action Summary

Claims in the application are 1-11.

The following is a quotation of the first paragraph of 35 U.S.C.

112:

5 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

 Claims 4, 5, 6, 7 and 9 are rejected under 35 U.S.C. 112, first
10 paragraph, because the specification, while being enabling for regenerating cartilage with human mesenchymal stem cells in an alginate gel as in claim 1, does not reasonably provide enablement for regenerating cartilage with an alginate gel not containing the cells as in claim 6, and for regenerating cartilage with the cells in contact with
15 the gel as in claims 4, 5 and 7, or the cells with the gel as in claim 9 instead of being in the gel. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

20 The specification fails to provide an enabling description for using the gel when not containing the cells to regenerate cartilage, or provide an enabling description of using cells in association with the gel other than the cells being in the gel.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

25 The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

 Claims 4, 5, 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is unclear by not having antecedent basis for "the construct" (line 2). Additionally, by requiring the cells to "contact" the gel as in claims 4, 5 and 7, it is unclear as to whether the cells are mixed with the gel, in the gel or are on the surface of the gel. Similarly, in claim 9, requiring the cells to be with the gel makes unclear as to the association of the cells with the gel.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 7 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Grande et al (WO 96/28539).

Claim 1 is drawn to a composition for producing cartilage comprising human mesenchymal stem cells in an alginate gel layer which supports differentiation and maturation of the cells into chondrocytes. Claim 6 is drawn to a composition for regenerating cartilage containing an alginate layer which supports differentiation and maturation of the cells into chondrocytes. Claims 7 and 9 are drawn to methods of regenerating or repairing cartilage by administering the cells with an alginate gel. Claims 10 and 11 are drawn to a method of regenerating or repairing

cartilage by administering the cells in a solution of alginate and solidifying the alginate *in vivo*.

Grande et al disclose (page 6, line 10 to page 7, line 9, and page 15) generating cartilage *in vivo* by forming an alginate solution containing human mesenchymal stem cells, injecting the solution where cartilage is to be generated, and gelling the alginate *in vivo*. Alternatively, the alginate may be gelled and the gelled alginate containing the cells implanted.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 7 and 9-11 rejected under 35 U.S.C. 103(a) as being unpatentable over Borland et al (WO 98/25653) in view of Grande et al.

The claimed invention and Grande et al are described above.

Borland et al (WO 98/25653) disclose forming a partially hardened alginate gel (page 13, lines 15-29, and paragraph bridging pages 18 and 19) containing cells such as cells that form cartilage (page 26, lines 1-2) and injecting the partially hardened gel to form cartilage.

5 It would have been obvious to replace the partially hardened alginate gel of Borland et al with an alginate solution and inject the solution, or with a hardened alginate gel and implant the hardened gel as disclosed by Grande et al when injecting an alginate solution or implanting an alginate gel to form cartilage since using the alginate
10 solution or gel would have been expected to provide the same type of result as when using partially hardened alginate gel. Using human mesenchymal stem cells as the cartilage forming cells of Borland et al would have been further suggested by Grande et al using human mesenchymal stem cells to form cartilage, and these cells would have been expected to
15 provide the function of cartilage forming cells desired by Borland et al.

Claims 2-5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grande et al in view of Pittenger et al (WO 98/32333).

Claim 2 requires the composition of claim 1 to contain hyaluronic acid. Claims 3 and 8 require the human mesenchymal stem cells to be in
20 contact with a chondroinductive agent, and claims 4 and 5 require inducing chondrogenesis in mesenchymal stem cells by contacting the cells with an alginate gel *in vitro*.

Pittenger et al disclose carrying out *in vitro* chondrogenesis of human mesenchymal stem cells in an alginate gel in contact with a

chondroinductive agent such as a component of extracellular matrix such as hyaluronic acid (page 15, line 8 of first full paragraph).

It would have been obvious to combine the human mesenchymal stem cells of Grande et al with a component of extracellular matrix such as
5 hyaluronic acid to obtain its chondroinductive function to induce differentiation of the human mesenchymal stem cells into chondrocytes as suggested by Pittenger et al. Pittenger et al would have further suggested carrying out chondrogenesis of mesenchymal stem cells *in vitro* when desiring to obtain chondrocytes for implanting.

10 Claims 2-5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borland et al in view of Grande et al as applied to claims 1, 6, 7 and 9-11 above, and further in view of Pittenger et al.

The claimed invention and references are described above.

When using an alginate solution or gel and human mesenchymal stem
15 cells in Borland et al as set forth above, it would have been obvious to combine the human mesenchymal stem cells with a component of extracellular matrix such as hyaluronic acid to obtain its chondroinductive function to induce differentiation of the human mesenchymal stem cells into chondrocytes as suggested by Pittenger et al.
20 Pittenger et al would have further suggested carrying out chondrogenesis of mesenchymal stem cells *in vitro* when desiring to obtain chondrocytes for implanting.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone
25 number is (703) 308-0520. The examiner can normally be reached on

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Monday-Thursday and every other Friday from about 8:30 AM to about 6:00 PM.

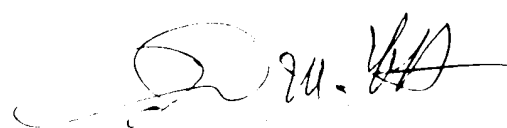
If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.

5 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number (703) 308-4743.

The fax phone number is (703) 872-9306 before final rejection or (703) 872-9307 after final rejection.

10 Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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DMN
8/30/02